

PRELIMINARY AMENDMENT

National Stage Entry of PCT/JP03/06959
Attorney Docket No.: Q835.79
December 3, 2004

AMENDMENTS TO THE SPECIFICATION

Please amend the last paragraph on page 110, bridging page 111, as follows:

A solution of 1.980 g (5 mmol) of (2R)-1-[4-(benzyloxy)phenyl]-2-[((1R)-phenethylmethoxyethyl)amino]-1-propanone hydrochloride (99.4% d.e.) synthesized as in EXAMPLE 15 and 500 mg of 10% Pd/C (containing 50% of water) in 20 mL of ethanol and 5 mL of water was stirred under a hydrogen atmosphere at 1 atm and 40°C for 20 hours. After the catalyst was filtered off, the solvents were distilled off under a reduced pressure to obtain 1.3281 g of a light-yellow, oily substance. To this substance, 30 mL of ethanol was added and condensed again. Subsequently, 1.5 mL of methanol and 15 mL of methylene chloride were added, and the resulting mixture was stirred at 5°C for 30 minutes to precipitate crystals. The crystals were filtered off under a reduced pressure. White crystals of (1S,2R)-1-(4-hydroxyphenyl)-2-amino-1-propanol hydrochloride were obtained as a result (747.8 mg, isolation yield :72%). The optical purity and the diastereomer ratio of this substance were determined by the method set forth in EXAMPLE 22. The optical purity was 100% e.e. The ratio, (1S,2R)-isomer/(1R,2R)-isomer, was 97.8/2.2.

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Please amend the last paragraph on page 111, bridging page 112, as follows:

A solution of 911 mg (2 mmol) of (2S)-1-[4-(benzyloxy)phenyl]-2-[(*(1R)-phenethyl*ethyl)amino]-1-propanone methanesulfonate (98.4% d.e.) synthesized as in EXAMPLE 3, 911 mg of 10% Pd/C (containing 50% of water) in 10 mL of ethanol was stirred under a hydrogen atmosphere at 1 atm and 40°C for 20 hours. After the catalyst was filtered off, the solvents were distilled off under a reduced pressure to obtain 652.4 mg of a light-yellow, oily substance. To this substance, 1 mL of ethanol and 5 mL of methylene chloride were added, and the resulting mixture was stirred at 5°C for 30 minutes to precipitate crystals. The crystals were filtered off under a reduced pressure. White crystals of (1*R*,2*S*)-1-(4-hydroxyphenyl)-2-amino-1-propanol methanesulfonate were obtained as a result (449.8 mg, isolation yield: 85%). The optical purity and the diastereomer ratio of this substance were determined by the method set forth in EXAMPLE 22. The optical purity was 98.6% e.e. The ratio, (1*R*,2*S*)-isomer/(1*S*,2*S*)-isomer, was 90.4/9.6.

¹H-NMR (DMSO, 400 MHz/ ppm): δ 0.92 (3H, d), 2.35 (3H, s), 3.32 (1H, m), 4.75 (1H, brs), 5.85 (1H, d), 6.75 (2H, d), 7.14 (2H, d), 7.78 (3H, brs), 9.38 (1H, s)